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QUANTIFYING SELECTION BIAS IN EPIDEMIOLOGIC STUDIES.

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As participation rates (P) in epidemiologic studies decline, it becomes increasingly important to quantify the influence of study parameters on the bias in the estimation of association parameters. We examine the non-participation bias ratio (NPBR), the ratio of the observed to true odds ratio (OR). In case-control studies, the NPBR usefully decomposes as the participation ratio in exposed versus unexposed cases (P_{D1E1} / P_{D1E0}) divided by that in controls (P_{D0E1} / P_{D0E0}). We refine understanding of selection bias by evaluating the effects of exposure prevalence, overall case and control P, and realistic participation differentials in cases ($P_{D1E1} - P_{D1E0}$) and controls ($P_{D0E1} - P_{D0E0}$) on NPBR. We demonstrate that the NPBR is robust to changes in exposure prevalence and only modestly affected by decreasing magnitude of P. Bias rapidly rises as the case participation differential diverges from the control participation differential. Let the overall P be 70% among both cases and controls and the prevalence of exposure be 5%. If the cases have no participation differential, the NPBR is 0.87 and 0.70 if the participation differential in controls is 10% and 30%, respectively. The NPBR changes little (NPBR=0.83 and 0.62) in the same scenario if the control P drops to 50%. If the participation ratios in the two examples were the same, then NPBRs would be identical. We present complete results for a range of scenarios demonstrating the effects of exposure prevalence, overall case and control participation, and realistic participation differentials on NPBR. In conclusion, a diverging participation differential among cases and controls, not difference in overall P or exposure prevalence, drives the selection bias. Although it is reassuring that low participation rates alone do not result in biased observed odds ratios, epidemiologists must focus on understanding the determinants of differential participation.

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SELECTION BIAS WHEN BIOPSIED CONTROLS ARE USED IN BIOMARKER RESEARCH.

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When tissue from controls is needed for research involving measurement of biomarkers, it is usually only feasible to get tissue from patients who underwent a procedure as part of a diagnostic evaluation for cancer or other diseases. This design poses an example of classic selection bias, in that controls do not represent the underlying population of normal individuals. To better understand this phenomenon, we compared the magnitude of risk associated with established risk factors for breast cancer in women with invasive breast cancer (n=1446) and women with proliferative benign breast disease (atypical hyperplasia, ductal hyperplasia, fibroadenoma, n=1292) relative to two control groups in a population-based setting: 1) biopsied benign/normal controls (BC, n=1216) and 2) mammographically negative, non-biopsied women (MC, n=65,718). Women were eligible for study if they underwent mammography between 1996 and 2001 at Group Health Cooperative, a large HMO based in Seattle, Washington. Women divided into the four groups described. For a number of risk factors, particularly high mammographic breast density, the risk of breast cancer or risk of proliferative benign disease was sharply attenuated when either case group was compared to biopsied controls (BC) versus mammographic negative, non-biopsied women (MC). For example, the relative risk of breast cancer associated with high breast density was 1.3 (0.8–2.2) when cases were compared to BC versus 3.0 (2.2–4.1) when cases were compared to MC. Risk of benign proliferative disease associated with high breast density was 1.2 (0.7–2.0) compared to BC and 2.8 (2.0–4.) compared to MC. All risk estimates were adjusted for age. If mammographic density is associated with different tissue biomarkers, these results suggest that those differences would not be observed had the benign/normal biopsied women served as controls. In contrast, large risk estimates could have been observed had randomly recruited healthy women donated breast tissue.

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STOCHASTIC CONSIDERATIONS IN NON-DIFFERENTIAL MISCLASSIFICATION AND BIAS IN ESTIMATION OF ODDS RATIOS.

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It is well known that non-differential misclassification with dichotomous exposures and outcomes will bias the odds ratio (OR) towards the null except in the presence of extreme degrees of misclassification. However, this conclusion is only valid in the population or when considering expected values for the OR. In actual studies, the misclassification observed will reflect stochastic misclassification processes in which each subject will be classified on exposure based on a probability of being misclassified. The observed distribution of subjects after misclassification may no longer show non-differential misclassification. We undertook a series of simulation studies to examine the distribution of the observed OR under non-differentiation misclassification of exposure. Factors examined were: probability of correctly classifying exposed subjects (0.7–0.99), probability of correctly classifying unexposed subjects (0.7–0.99), sample size (150, 300 and 1,000), true OR (1.5/2.5) and overall exposure prevalence (25%, 50% and 75%). The probability of over-estimating the true OR ranged up to 35% and was higher for smaller studies and for those with a lower true OR. Studies with low misclassification displayed a higher probability of over-estimating the OR although the magnitude of the over-estimation was generally small (10–15%). Exposure prevalence had little impact on the probability of over-estimation but did influence whether misclassification of exposed or unexposed subjects had the largest impact. These results should be used in claiming that OR estimates in the presence of non-differential mis-

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PREDICTORS AND CONSEQUENCES OF ATTRITION IN A COHORT OF OLDER WOMEN WITH BREAST CANCER.

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Background: All cohort studies that require repeated contact with study participants might be subject to attrition bias because not all of the participants complete the study. Studies in which the outcome of interest is a disease with significant morbidity are particularly vulnerable since the outcome itself might be a predictor of attrition. Objective: We examined the impact of morbidity on attrition in a cohort of older women with breast cancer in which 34% of the women who completed the baseline interview 3-months after their diagnosis did not complete a follow-up interview two years later. Methods: We enrolled a cohort of 867 women diagnosed with early stage breast cancer between 1996 and 1999. We used two sources of data to predict attrition: 1) baseline interview data and 2) inpatient Medicare claims files for the two years after the baseline interview. The baseline interview contained data on demographics, physical function and health, mental health and social support. Inpatient Medicare claims data were obtained from the Medicare Provider Analysis and Review data files from 1997 through 2001. Results: Using data from our baseline interview, we observed that older women were 1.7-fold more likely to not complete the follow-up interview (95% confidence interval (CI): 1.2, 2.6) and women who reported poor mental health, as measured by the lowest quartile of scores on the 5 Item Mental Health Index, were greater than two-fold more likely not to complete the follow-up interview (OR: 2.2, 95% CI: 1.4, 3.4). Women with any hospitalization in the two years after their baseline interview were 2.5-

low-up interview (95% CI: 1.4, 4.5). Conclusions: This data suggests that inpatient hospitalization is a